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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/747,538	12/21/2000	David Aaron Katz	6652.US.01	2085

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/747,538	KATZ ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,18,38-40 and 43-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-18, 38-40, 43-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action filed on June 30, 2006 has been entered.

Status of the Application

2. Claims 17-18, 38-40, 43-47 are pending and claims 1-16, 19-37, 41-42 are cancelled. New claims 44-47 are added. All amendments and arguments have been thoroughly reviewed and deemed persuasive for the reasons that follow. This action is made Non-final.

New Grounds of Rejections

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 38-40, 43-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Steen et al. (Pharmacogenetics, Vol. 5, pp. 215-223, 1995).

Steen et al. teach a method of claim 38, for detecting a target nucleic acid sequence suspected of having deletion of at least 50 base pairs (13kb gene deletion) in a test sample comprising

(a) contacting the test sample with amplification reagents comprising amplification primer (see page 217, col. 2, paragraph 1 under PCR-based gene deletion assay);

(b) subjecting the reaction mixture to amplification conditions to form a target nucleic acid sequence amplification product and a standard nucleic acid amplification product (see page 217, col. 2, paragraph 1 under PCR-based gene deletion assay);

(c and d) detecting a first and second signal corresponding to a deletion and a standard nucleic acid (13kb deletion and a standard 3.5 kb nucleic acid) (see page 220, Fig. 3);

(e) comparing the first and second signals to determine a deletion or insertion of at least 50 base pairs is present in the DNA in the test sample (see page 220, Fig. 3, col. 1, line 4-13 of paragraph 1, co. 2, paragraphs 1-2), wherein the amplification reagents comprise one primer that hybridizes to both the target and the standard nucleic acid sequence (see page 220, Fig. 3, legend states that the primers CYP-13 and CYP-24 were designed to amplify a 3.5kb product in the presence of the 13kb gene deletion allele indicating primers in the amplification reagent hybridize to both target deletion and standard nucleic acid sequence).

With regard to claim 39-40, Steen et al. teach that the deletion is of 13kb (which includes the limitation of claims 39-40) (see page 215, abstract, page 220, Fig. 3, col. 1, paragraph 1);

With regard to claim 43, Steen et al. teach that the deletion is in the CYP2D6 locus, which is a polymorphic (see page 216, col. 1, paragraphs 1-2, col. 2, paragraphs 1-2).

With regard to claim 44, Steen et al. teach that the amplification reagents comprise a polymerase (see page 217, col. 2, paragraph 1 under PCR-based gene deletion assay).

With regard to claim 45, Steen et al. teach that the amplification conditions comprise denaturation cycle above 90^0 C, annealing temperature cycle between 45^0 to 65^0 C and raising temperature of the reaction to a temperature sufficient to activate the polymerase (synthesis or

extension cycle) (see page 217, col. 2, paragraph 1 under PCR-based gene deletion assay). Accordingly the instant claims are anticipated by Steen et al.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 17-18, and 46-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over (Pharmacogenetics, Vol. 5, pp. 215-223, 1995) in view of Wittwer et al. (USPN. 6,232,079).

Steen et al. teach a method of claim 38, for detecting a target nucleic acid sequence suspected of having deletion of at least 50 base pairs (13kb gene deletion) in a test sample comprising

(a) contacting the test sample with amplification reagents comprising amplification primer (see page 217, col. 2, paragraph 1 under PCR-based gene deletion assay);

(b) subjecting the reaction mixture to amplification conditions to form a target nucleic acid sequence amplification product and a standard nucleic acid amplification product(see page 217, col. 2, paragraph 1 under PCR-based gene deletion assay);

(c and d) detecting a first and second signal corresponding to a deletion and a standard nucleic acid (13kb deletion and a standard 3.5 kb nucleic acid) (see page 220, Fig. 3);
(e) comparing the first and second signals to determine a deletion or insertion of at least 50 base pairs is present in the DNA in the test sample (see page 220, Fig. 3, col. 1, line 4-13 of paragraph 1, co. 2, paragraphs 1-2), wherein the amplification reagents comprise one primer that hybridizes to both the target and the standard nucleic acid sequence (see page 220, Fig. 3, legend states that the primers CYP-13 and CYP-24 were designed to amplify a 3.5kb product in the presence of the 13kb gene deletion allele indicating primers in the amplification reagent hybridize to both target deletion and standard nucleic acid sequence).

Steen et al. also teach that the deletion is of 13kb (which includes the limitation of claims 39-40) (see page 215, abstract, page 220, Fig. 3, col. 1, paragraph 1); the deletion is in the CYP2D6 locus, which is a polymorphic (see page 216, col. 1, paragraphs 1-2, col. 2, paragraphs 1-2). With regard to claim 44, Steen et al. teach that the amplification reagents comprise a polymerase (see page 217, col. 2, paragraph 1 under PCR-based gene deletion assay); the amplification conditions comprise denaturation cycle above 90^0 C, annealing temperature cycle between 45^0 to 65^0 C and raising temperature of the reaction to a temperature sufficient to activate the polymerase (synthesis or extension cycle) (see page 217, col. 2, paragraph 1 under PCR-based gene deletion assay). However Steen et al. did not teach use of a probe in amplification reaction.

Wittwer et al. teach a method for monitoring hybridization during PCR (real-time PCR) for detecting a target nucleic acid sequence in a test sample comprising (a) contacting the test sample with amplification reagents comprising a polymerase, a PCR primer pair, and a probe (see column 6, lines 1-15, column 44, lines 24-38); (b) performing PCR cycles (i) raising temperature to dissociate the double-stranded genomic DNA, lowering the temperature to allow primers and probe to hybridize to the target nucleic acid, raising the temperature to dissociate the target-probe hybrids and extending the primers and continuously raising the temperature to temperature dependent polymerase extension (see column 44, lines 50-67, column 45, lines 1-12); (c) repeatedly performing the PCR cycles to form an amplification product (see column 45, lines 13-53) and (d) detection of the amplification product as an indication of presence of the nucleic acid (see column 45, lines 13-53).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine the method of amplification of a target nucleic acid as taught by Steen et al. with the step of primer extension in the presence of a probe or monitoring hybridization during PCR as taught by Wittwer et al. to achieve expected advantage of developing a sensitive and enhanced method for amplification of a specific target. An ordinary skill in the art would have reasonable expectation of success that the modification of the method taught by Steen et al. with the step of monitoring hybridization during PCR would result in continuously monitoring of DNA amplification, identification and quantitation of the target nucleic acid and reducing laborious processing steps after PCR to identify the said target nucleic acid (see col. 3, line 14-33 of Wittwer et al. patent) and such modification of the method is considered obvious over the cited prior art in the absence of secondary considerations.

Response to arguments:

5. With regard to the rejection of claim 41 under 35 USC 112, second paragraph, Applicants' arguments and amendment are fully considered and the rejection is withdrawn herein, in view of the amendment.

6. With regard to the rejection of claim 41 under 35 USC 101, Applicants' arguments and amendment are fully considered and the rejection is withdrawn herein, in view of the amendment.

7. With regard to the rejection of claims 38-40, 43 under 35 USC 102(b) as being anticipated by Evans et al., Applicants' arguments and amendment are fully considered and the rejection is withdrawn herein, in view of persuasive arguments and new grounds of rejections.

8. With regard to the rejection of claims 41 under 35 USC 103(a) as being obvious over Evans et al. in view of Van Ness et al. Applicants' arguments and amendment are fully considered and the rejection is withdrawn herein, in view of the persuasive arguments and new grounds of rejections.

9. With regard to the rejection of claims 17-18 under 35 USC 103(a) as being obvious over Evans et al. in view of Van Ness et al. and Wittwer et al. Applicants' arguments and amendment are fully considered and the rejection is withdrawn herein, in view of the persuasive arguments and new grounds of rejections.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Primary Examiner
Art Unit 1637

Prabha Chunduru 9/11/06
SURYAPRABHA CHUNDURU
PATENT EXAMINER